UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,186	07/20/2001	Leonard A. Smith	A33626A 067252.0107	8442

21003 7590 06/03/2003

BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	15

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/910,186	Smith et al
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sh et with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 7, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *42-51, 53-56, 82, 85, and 86* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *42-51, 53-56, 82, 85, and 86* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 14
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 42-49,53,55-56,82 and 85-86 have been amended.

Claims 42-51, 53-56, 82 and 85-86 are under consideration.

Claims 1-38, 39-41,52,54,57-79,80-81 and 83-84 have been canceled.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

SEQUENCE COMPLIANCE

2. Applicant has submitted SEQ ID Nos for the sequences in the instant specification.

Information Disclosure Statement

3. The information disclosure statement (PTO-1449) filed March 7~~6~~, 2003 has been considered.

Objections/Rejections Withdrawn

4. The drawings objected to because the Brief Description of the drawings does not refer to the multiple frames shown in each figure, specifically Figure 1, A&B etc, has been obviated in light of the amendment of the Brief Description of the Drawings to describe the embodiments set forth in each drawing.
5. Claims 43, 48-51 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, in light of the amendment of the claims to recite SEQ ID NO 8, and to no longer recite the phrase the term "portions".
6. Claims 43, 48-51 rejected under 35 U.S.C. 112, first paragraph, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, in light of the amendment of the claims to require the nucleic acid to encode a polypeptide of SEQ ID NO 8.
7. Claim 54 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, in light of the cancellation of claim 54.

8. Claims 39-51, 54-56, 82, 85 and 86 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the cancellation of some claims and amendment of others to clearly set forth Applicant's claimed invention.

9. Claims 39-47, 54-56, 82-86 are rejected under 35 U.S.C. 102(a) as being anticipated by Campbell et al (September 1993), in light of the amendment of the claims to require the claimed nucleic acid to encode SEQ ID NO 8, and not just a portion of SEQ ID NO 8.

10. Claims 39, 41, 48 and 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Smith (different inventive entity, priority date for yeast/Pichia pastoris claims is not 1993), , in light of the amendment of the claims to require the claimed nucleic acid to encode SEQ ID NO 8, and not just a portion of SEQ ID NO 8.

11. Claims 39-47, 54-56, 82-86 are rejected under 35 U.S.C. 102(a) as being anticipated by Halpern et al (May 1993),, in light of the amendment of the claims to require the claimed nucleic acid to encode SEQ ID NO 8, and not just a portion of SEQ ID NO 8.

12. Claims 39-47, 53 and 54 (in so far as the claims are being read to include any serotype of heavy chain of botulinum toxin, to include serotype B), 55-56, 82, 85-86 are rejected under 35 U.S.C. 102(b) as being anticipated by Whelan, SM et al (May 28, 1992; Accession number M81186), in light of the amendment of the claims to require the claimed nucleic acid to encode SEQ ID NO 8, and not just a portion of SEQ ID NO 8.

13. Claims 39-50,53-56, 82,85-86 are rejected under 35 U.S.C. 102(b) as being anticipated by Jung et al (Feb. 1992), in light of the amendment of the claims to require the claimed nucleic acid to encode SEQ ID NO 8, and not just a portion of SEQ ID NO 8.

14. Claims 39-47, 55-56 are rejected under 35 U.S.C. 102(e) as being anticipated by Williams, James A(US Pat. 5,919,665), in light of the amendment of the claims to require the claimed nucleic acid to encode SEQ ID NO 8, and not just a portion of SEQ ID NO 8.

Rejections Maintained

15. Claims 39-43, 45-47, 55-56 rejected under 35 U.S.C. 101, (non-statutory subject matter) not directed to isolated and purified nucleic acid molecules and therefore read on a product of nature; the claimed invention is directed to non-statutory subject matter.

16. Claims 42-51, 53-56, 82 and 85-86 as previously applied to claims 39-42, 43, 44-51, 55-56, 82, 85-86 rejected under 35 U.S.C. 112, first paragraph,*written description* as containing subject matter which was not described in the specification in such a full, clear, concise way, and exact terms or in sufficient detail as to reasonably convey to one skilled in the relevant art that can reasonably conclude that applicant had possession of the claimed invention at the time of filing, for reasons of record in paper number11, paragraph 15.

17. Claim 53 rejected under 35 U.S.C. 112, second paragraph, for not reciting a combination of methods steps that correlate with the recited intended use of the method set forth in the preamble of the claim "A method of preparing an immunogenic composition", for reasons of record in paper number 11, paragraph 19, page 14.

Response to Arguments

18. The rejection of claims 42-43, 45-47, 55-56 under 35 U.S.C. 101, (non-statutory subject matter) not directed to isolated and purified nucleic acid molecules and therefore read on a product of nature is traversed on the grounds that SEQ ID NO 8 is not a naturally occurring sequence.

19. It is the position for the examiner that natural variation at nucleic acid and amino acid levels for the same or equivalent proteins is common in nature. Amendment of the claim to recite --A non-naturally occurring-- or --A synthetic nucleic acid-- would be commensurate in scope with the instantly claimed invention and could obviate this rejection.

20. The rejection of 42-51, 53, 55-56, 82 and 85-86 as previously applied to claims 39-42, 43, 44-51, 55-56, 82, 85-86 under 35 U.S.C. 112, first paragraph *written description*, as

containing subject matter which was not described in the specification in such a full, clear, concise way, and exact terms or in sufficient detail as to reasonably convey to one skilled in the relevant art that applicant had possession of the claimed invention at the time of filing is traversed on the grounds that claims 39-41 have been canceled, claim 43 has been amended to independent form and asserts that Example 8 and Figure 4 provide support for the amended claims.

21. It is the position of the examiner that the nucleic acid of Example 8 (SEQ ID NO 40) does not encode the amino acid sequence of, nor comprise SEQ ID NO 8 (Figure 4), nor does SEQ ID NO 8 (Figure 4) comprise the nucleic acid of Example 8(SEQ ID NO 40). Example 8 and Figure 4 do not define a representative number of species of the instantly claimed genus of nucleic acid molecules that comprise the nucleic acid that encodes the sequence of SEQ ID NO 8. The lack of written description is maintained for reasons of record in paper number 11, paragraph 15.

22. The rejection of claim 53 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reciting methods steps (culturing and recovering) that do not correspond to the recited preamble which is directed to a method of preparing an immunogenic composition is traversed on the grounds that the method of claim 53 has been amended to recite the step of "recovering from said transfected cell at least one insoluble polypeptide" which is asserted to correspond to the preamble of the claimed invention.

23. It is the position of the examiner that claim 53 is not a Jepson claim, that defines new methods step in a method of preparing an immunogenic composition. No preparing step of any immunogenic compositions is recited, only the host organism is cultured and a polypeptide recovered. Recovery of a polypeptide is not a preparing step for an immunogenic composition. Amendment of the claim to recite Jepson format, to recite a --method of recovering a polypeptide-- or to recite a --preparing-- step could obviate this rejection. The method is not distinctly claimed.

New Claim Limitations/New Grounds of Rejection

Improper Incorporation by Reference

24. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

25. SEQ ID Nos have been amended based upon accession number M81186, to Whelan et al , a publication, the disclosure of which has not been fully or properly incorporated by reference. Changes of SEQ ID Nos based upon disclosure in a publication improperly incorporated by reference would constitute New Matter.

Claim Rejections - 35 U.S.C. § 112

26. The amendment filed March 7, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

i. SEQ ID No 37 has been amended to recite changes based upon other sequences as shown in Figure 1, 2 and 3, which are all synthetic coding sequence and are not taught to be identical to one another, nor to encode the same polypeptides. SEQ ID NO 37 has been amended to recite nucleotides present in the synthetic coding sequences of Figures 1, 2 and 3, but the disclosure at page 37 of the instant specification does not teach ~~the~~ that SEQ ID No 37 corresponds to or is intended to evidence the same sequences as the sequences shown in Figures 1, 2 and 3. The sequences of Figures 1, 2 and 3 are not identical to one another by being of differing sequences and comprising differing numbers of nucleic acids; nor are the sequences of Figures 1, 2 and 3 identical to SEQ ID NO 37. Each sequence sets forth a different nucleotide sequence which have been disclosed to evidence differing numbers of nucleotides for synthetic nucleic acid sequences. One sequence does not provide original descriptive support for the others as each coding sequence is distinct. Newly submitted SEQ ID NO 37 has been modified from what was originally described in the instant specification. The specification comprises New Matter due to the changes introduced into SEQ ID NO 37 which do not evidence original descriptive support in the instant specification.

ii. Figure 4, and SEQ ID NO 39 have been modified through deletion, addition and substitution of nucleic acids at positions defined at page 55, of the Amendment submitted March 7, 2003. SEQ ID NO 39 is a synthetic coding sequence that would not be expected to identical to the naturally occurring Hc fragment botulinum neurotoxin B. Changes in the originally described synthetic nucleic acid coding sequence set forth at pages 38-39 does not find original descriptive support in the synthetic coding sequence shown in Figure 4; Figure 4 and SEQ ID No 39 set forth different sequences . Figure 4 is not discussed at pages 38-39, nor are pages 38-39 discussed in the Brief Description of the Drawings. The instant specification discloses a number of synthetic coding sequences that do not have the same nucleic acid sequences. The nucleic acid sequences set forth in Figure 4, and at page 38-39 do not provide original descriptive support for changes introduced into each of these sequences as these two sequence were not disclosed to be the same synthetic sequence. The changes introduced into the sequences of Figure 4 and SEQ ID NO 39 constitute New Matter.

iii. SEQ ID NO 40 has been amended based upon nucleic acid accession number M81186, which has not been disclosed in the instant specification. Changes made to SEQ ID NO 40 based upon improper incorporation by reference constitutes New Matter. SEQ ID NO 8 and SEQ ID NO 40 have not been described to the identical sequences, therefore, SEQ ID NO 8 does not provide original descriptive support for changes to SEQ ID NO 40 which is a different sequence.

iv. SEQ ID NO 41 has been changed based upon sequences shown in Figures 1,2, 3 and SEQ ID NO 38, which are not identical to SEQ ID NO 41. SEQ ID NO 41 is taught to deduced from a series of references at page 12 of the instant specification. Improper incorporation by reference to material essential to support for changes in the disclosed sequence of SEQ ID NO 41, constitutes New Matter.

v. SEQ ID NO 42 has been changed based upon sequences shown in Figure 4 (SEQ ID NO 8) and accession number M81186. SEQ ID NO 8 is not identical to SEQ ID NO 42 and is not taught to be support for SEQ ID NO 42. Improper incorporation by reference to material essential to support for changes in the disclosed sequence of SEQ ID NO 42, constitutes New Matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

27. Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 43 has been amended to recite the phrase "said amino acid sequence comprising at least one immunogenic epitope". It is not clear from the claim language recited whether the immunogenic epitope is heterologous to SEQ ID NO 8 or is inherent to SEQ ID NO 8, as the claimed nucleic acid comprises ("having" is being read as "open" language) the nucleotide sequence for SEQ ID NO 8, but what additional amino acid sequences the claimed nucleic acid encodes and the source of the immunogenic epitope are not distinctly claimed. Clarification of what the immunogenic epitope is, is requested.

Claim Objections

28. Claim 42 is objected to because of the following informalities: Claim 42 depends from later claim 43; claims should depend from an earlier, smaller numbered claim. Appropriate correction is required.

Double Patenting

29. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

30. Claims 45,48, 53, 82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4,8,13-16,23 of U.S. Patent No. 6,495,143. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention is directed to a genus of nucleic acids that comprise an expression control sequence operably linked to the nucleic acid, which defines a genus of expression vectors(instant claim 45) which are incorporated and host cells (instant claim 82) that encode BoNTB and the allowed claims are directed to a species (allowed claims 1-4, 8: a vector VEE being the expression control sequence for the nucleic acid encoding the carboxy terminal of BoNTB); the expression vector is incorporated into a species of host cell, specifically a prokaryotic or eukaryotic host cell expression vector (see allowed claims 13-15); and the host cell is used in a method of producing a polypeptide (instant claims 48 and 53) which are obvious over the allowed claims 16 and 23. A genus is obvious over a species; the allowed species anticipates the instantly claimed genus.

Conclusion

31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
May 29, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual - ePAVE)

2. Mailed to:
Commissioner for Patents
P.O. Box 22313-1450
Alexandria, VA 22313-1450

3. Hand Carried directly to:
U. S. Patent and Trademark Office
Technology Center 1600, Reception Area 7th Floor
Examiner Name
Sequence Information
Crystal Mall One
1911 South Clark Street
Arlington, VA 22202

4. Hand Carried directly to the Customer Window at:
U. S. Patent and Trademark Office
Box Sequence, Customer Window, Lobby, Room 1B03
Crystal Plaza Two
2011 South Clark Place
Arlington, Virginia 22202

5. Mailed by Federal Express, United Parcel Service or other delivery service to:
U. S. Patent and Trademark Office
Box Sequence, Room 1B03-Mailroom
Crystal Plaza Two
2011 South Clark Place
Arlington, Virginia 22202